Efficacy of cardiac autonomic denervation for atrial fibrillation: a meta-analysis

CRD summary
This review concluded that compared to pulmonary vein isolation (PVI), cardiac autonomic denervation plus PVI improved atrial fibrillation rates in paroxysmal and non-paroxysmal atrial fibrillation. Cardiac autonomic denervation/ganglionated plexi ablation alone was inferior to PVI alone. There were questions about quality of included data, some review methods and inconsistencies in reporting. The reliability of conclusions is unclear.

Authors' objectives
To assess whether adjunctive cardiac autonomic denervation added to pulmonary vein isolation was effective for the elimination of atrial fibrillation and whether cardiac autonomic denervation alone was superior to pulmonary vein isolation.

Searching
MEDLINE (to February 2011), EMBASE (to 2010) and Cochrane Central Register of Controlled Trials (CENTRAL) (2010) were searched for studies published in English or Chinese. Search terms were reported. Abstracts of four relevant scientific sessions (2001 to 2011) and bibliographies were checked for further studies. Only published studies were eligible for inclusion.

Study selection
Controlled trials in people with atrial fibrillation with at least three months follow-up that compared cardiac autonomic denervation/ganglionated plexi ablation to pulmonary vein isolation or cardiac autonomic denervation/ganglionated plexi ablation plus pulmonary vein isolation to pulmonary vein isolation alone were eligible for inclusion. The primary outcome of interest appeared to be rate of freedom from atrial fibrillation or other atrial arrhythmias. Complications were reported (bleeding/vascular complications, pericardial effusion/tamponade, pulmonary vein stenosis, pericarditis, haemoptysis dyspnoea, prolonged asystole).

The included studies were described as randomised controlled (RCTs) and non-RCTs. Mean ages ranged from 49 to 62 years. From 16% to 88% of the participants were men. Reported durations of atrial fibrillation ranged from four to 8.4 years. Most participants had paroxysmal atrial fibrillation but in some studies some or all participants did not. Mean left ventricular ejection fraction ranged from 52% to 62% and left atrial diameter 40mm to 47mm. There were some variations in ablation techniques. Participants in some studies had repeat ablations. In most studies antiarrhythmic drugs were used post-ablation (to two to three months).

Two reviewers independently selected studies for inclusion. Discrepancies were resolved by consensus.

Assessment of study quality
The authors did not state that they assessed quality.

Data extraction
Data were extracted in order to calculate odds ratio (OR) and 95% confidence intervals (CI).

The authors did not state how many of them performed the data extraction.

Methods of synthesis
Pooled odds ratio and 95% confidence intervals were calculated using a random-effects model. Heterogeneity was assessed using the Q statistic and $I^2$. Subgroup analyses were based on type of atrial fibrillation (paroxysmal, non-paroxysmal) and type of ablation (cardiac autonomic denervation, ganglionated plexi ablation). Sensitivity analyses investigated study design (RCT, non-RCT) and length of follow-up (≥10 months).

Funnel plots were used to assess publication bias.
Results of the review
Fifteen studies (1,147 participants, range 38 to 200) were included: nine RCTs (664 participants) and six non-RCTs (550 participants). Follow-up ranged from three to 18 months. Funnel plots showed no evidence of publication bias.

Cardiac autonomic denervation/ganglionated plexi ablation was inferior to pulmonary vein isolation for rate of freedom from atrial fibrillation (OR 0.31, 95% CI 0.11 to 0.86; I²=77%; five studies). In subgroup analyses for people with paroxysmal atrial fibrillation, pulmonary vein isolation was superior to cardiac autonomic denervation/ganglionated plexi ablation (OR 0.18, 95% CI 0.10 to 0.33) but there was no difference for those with non-paroxysmal atrial fibrillation. Complications were reported in four people in the intervention groups and five in the control groups.

Compared to pulmonary vein isolation alone, cardiac autonomic denervation/ganglionated plexi ablation plus pulmonary vein isolation was associated with an improvement in freedom from atrial fibrillation (OR 1.85, 95% CI 1.33 to 2.59; I²=17%; 10 trials). Subgroup analyses results were similar to the main analyses for those with paroxysmal atrial fibrillation (I²=0%) and non-paroxysmal atrial fibrillation (I²=43%) and for comparisons between subgroups of cardiac autonomic denervation (I²=15%) and ganglionated plexi ablation. Complications were reported in nine people in the intervention group and eight in the control group. No deaths were reported.

Sensitivity analyses showed similar results to the main analyses for RCTs and non-RCTs and when only studies with follow-up of 10 months or more were included.

Authors' conclusions
Cardiac autonomic denervation plus pulmonary vein isolation significantly increased freedom from atrial fibrillation after a single procedure both in paroxysmal and non-paroxysmal atrial fibrillation. Cardiac autonomic denervation/ganglionated plexi ablation alone was not superior to pulmonary vein isolation alone. The long-term benefit and risk of adjunctive autonomic denervation ablation deserved further evaluation.

CRD commentary
The aims of the review in terms of inclusion criteria for participants and treatments were clearly stated but were less clear for study designs. The search was limited to published studies in English and Chinese so language and publication biases may have affected the review; tests for publication bias were likely to be unreliable given the limited number of included studies. The authors used methods to reduce reviewer error and bias during study selection; methods used for data extraction were unclear. Study quality was not assessed so it was difficult to comment on the validity of included data.

It may not have been appropriate to combine data from different study designs and some of the included data appeared to have come from observational studies (generally considered to be of lower quality). Studies were generally small. Some subgroup analyses were based on data from small numbers of participants. There was a lack of detail about concomitant diseases and treatments and this may affect the generalisability of the review. There were some errors in reporting of numbers, confused labelling of directions of treatment effects in forests plots and confusion in use of terminology.

Questions about the quality of included data and some methods of the review and inconsistencies in reporting make the reliability of conclusions unclear.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that further studies with longer follow-up were needed to assess the effects of adding cardiac autonomic denervation to pulmonary vein isolation for treating atrial fibrillation and to compare the two treatments in people with paroxysmal atrial fibrillation.

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